

CLAIMS

We claim:

- 5
1. An isolated nucleic acid molecule comprising a nucleotide sequence encoding NIP45 or a biologically active portion thereof.
 2. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least 60 % homologous to the amino acid sequence of SEQ ID NO: 2 and interacts with the Rel Homology Domain of an NF-AT family protein.
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 3. The isolated nucleic acid molecule of claim 2, wherein the protein comprises an amino acid sequence at least 70 % homologous to the amino acid sequence of SEQ ID NO: 2.
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 4. The isolated nucleic acid molecule of claim 2, wherein the protein comprises an amino acid sequence at least 80 % homologous to the amino acid sequence of SEQ ID NO: 2.
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 5. The isolated nucleic acid molecule of claim 2, wherein the protein comprises an amino acid sequence at least 90 % homologous to the amino acid sequence of SEQ ID NO: 2.
 - 25
 6. An isolated nucleic acid molecule at least 15 nucleotides in length which hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.
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 7. The isolated nucleic acid molecule of claim 6 which comprises a naturally-occurring nucleotide sequence.
 8. The isolated nucleic acid molecule of claim 6 which encodes mouse NIP45.
 9. The isolated nucleic acid molecule of claim 6 which encodes human NIP45.
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 10. An isolated nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1.
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11. The isolated nucleic acid molecule of claim ~~10~~, comprising the nucleotide sequence of SEQ ID NO: 1.

5 12. An isolated nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 2.

13. An isolated nucleic acid molecule encoding a NIP45 fusion protein.

10 14. An isolated nucleic acid molecule which is antisense to the nucleic acid molecule of claim ~~1~~.

15 15. An isolated nucleic acid molecule which is antisense to the coding strand of a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.

16. The isolated nucleic acid molecule of claim ~~15~~ which is antisense to a coding region of the coding strand of the nucleotide sequence of SEQ ID NO: 1.

20 17. The isolated nucleic acid molecule of claim ~~15~~ which is antisense to a noncoding region of the coding strand of the nucleotide sequence of SEQ ID NO: 1.

18. A vector comprising the nucleic acid molecule of claim 1.

19. The vector of claim ~~18~~, which is a recombinant expression vector.

25 20. The vector of claim ~~19~~, which encodes a protein comprising the amino acid sequence of SEQ ID NO: 2.

30 21. The vector of claim ~~19~~, which comprises the coding region of the nucleotide sequence of SEQ ID NO: 1.

22. A host cell containing the vector of claim ~~18~~.

23. A host cell containing the recombinant expression vector of claim ~~19~~.

35 24. A method for producing NIP45 protein comprising culturing the host cell of claim ~~23~~ in a suitable medium until NIP45 protein is produced.

25. The method of claim 24, further comprising isolating NIP45 protein from the medium or the host cell.

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1 ~~26.~~ An isolated NIP45 protein or a biologically active portion thereof.

2 ~~27.~~ An isolated protein which comprises an amino acid sequence at least 60 %
5 homologous to the amino acid sequence of SEQ ID NO: 2 and interacts with the Rel
Homology Domain of an NF-AT family protein.

3 ~~28.~~ The isolated protein of claim ~~27~~², which is at least 70% homologous to the
amino acid sequence of SEQ ID NO: 2.

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4 ~~29.~~ The isolated protein of claim ~~27~~², which is at least 80% homologous to the
amino acid sequence of SEQ ID NO: 2.

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5 ~~30.~~ The isolated protein of claim ~~27~~², which is at least 90% homologous to the
amino acid sequence of SEQ ID NO: 2.

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6 ~~31.~~ A fusion protein comprising a NIP45 polypeptide operatively linked to a
non-NIP45 polypeptide.

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7 ~~32.~~ An antigenic peptide of NIP45 comprising at least 8 amino acid residues of
the amino acid sequence shown in SEQ ID NO: 2, the peptide comprising an epitope of
NIP45 such that an antibody raised against the peptide forms a specific immune complex
with NIP45.

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33. An antibody that specifically binds NIP45 protein.

34. The antibody of claim 33, which is a monoclonal antibody.

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35. The antibody of claim 34, which is coupled to a detectable substance.

36. A pharmaceutical composition comprising the antibody of claim 34 and a
pharmaceutically acceptable carrier.

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~~37. A nonhuman transgenic animal that contains cells carrying a transgene
encoding NIP45 protein.~~

~~38. The nonhuman transgenic animal of claim 37, which contains cells having
an altered endogenous NIP45 gene.~~

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8 ~~39~~. A method for identifying a compound that modulates an interaction between NIP45 and an NF-AT family protein, comprising:

a) combining:

(i) NIP45, or an NF-AT-interacting portion thereof; and

5 (ii) an NF-AT family protein, or a NIP45-interacting portion thereof;
in the presence and absence of a test compound;

b) determining the degree of interaction between (i) and (ii) in the presence and absence of the test compound; and

c) identifying an agent that modulates an interaction between NIP45 and an NF-AT
10 family protein.

9 ~~40~~. The method of claim ~~39~~⁸, wherein the NIP45-interacting portion of the NF-AT family protein comprises the Rel Homology Domain of the NF-AT family protein.

41. The method of claim ~~39~~⁸, wherein the degree of interaction between (i) and (ii) is determined by labeling (i) or (ii) with a detectable substance, isolating non-labeled (i) or (ii) and quantitating the amount of labeled (i) or (ii) that has become associated with non-labeled (i) or (ii).

20 11 ~~42~~. The method of claim ~~39~~⁸, wherein the test compound increases the degree of interaction between (i) and (ii), as compared to the degree of interaction in the absence of the test compound, and the test compound is identified as an agent that stimulates an interaction between NIP45 and an NF-AT family protein.

25 12 ~~43~~. The method of claim ~~39~~⁸, wherein the test compound decreases the degree of interaction between (i) and (ii), as compared to the degree of interaction in the absence of the test compound, and the test compound is identified as an agent that inhibits an interaction between NIP45 and an NF-AT family protein.

30 44. A method for identifying a compound that modulates the expression or activity of NIP45 comprising:

a) preparing an indicator cell, wherein said indicator cell contains:

i) a recombinant expression vector encoding NIP45; and

35 ii) a vector comprising regulatory sequences of a Th2-associated cytokine gene operatively linked a reporter gene;

b) contacting the indicator cell with a test compound;

c) determining the level of expression of the reporter gene in the indicator cell in the presence of the test compound;

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d) comparing the level of expression of the reporter gene in the indicator cell in the presence of the test compound with the level of expression of the reporter gene in the indicator cell in the absence of the test compound; and

e) identifying a compound that modulates the expression or activity of NIP45.

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45. A method for identifying a protein that interacts with NIP45 comprising:

a) providing a two hybrid assay including a host cell that contains:

i) a reporter gene operably linked to a transcriptional regulatory sequence;

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ii) a first chimeric gene that encodes a first fusion protein, said first fusion protein including NIP45;

iii) a library of second chimeric genes that encodes second fusion proteins;

15 wherein expression of the reporter gene is sensitive to interactions between the first fusion protein, the second fusion protein and the transcriptional regulatory sequence;

b) determining the level of expression of the reporter gene in the host cell;

and

c) identifying a protein that interacts with NIP45.

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